(A) *Working standard solution.* Transfer about 12.5 milligrams of 5-mercapto-1-methyl-1*H*-tetrazole (MMT) and an amount of cefpiramide working standard equivalent to about 25 milligrams of cefpiramide activity, both accurately weighed, to a 100-milliliter volumetric flask. Dissolve and dilute to volume with 0.03*M* phosphate buffer. Further dilute 2.0 milliliters of this solution to 100 milliliters with mobile phase.

(B) *Sample solution.* Transfer about 25 milligrams of the test material, accurately weighed, to a 50-milliliter volumetric flask. Dissolve and dilute to volume with mobile phase.

(iii) *Calculations.* Calculate the percentages, individually, of MMT and any other compounds detected as follows:

$$T_1 = \text{Percent MMT (tetrazole)} = \frac{A_u \times C_s \times P_s \times 100}{A_s \times C_u \times 1{,}000}$$

$$T_2 = \text{Percent related compound} = \frac{R_u \times C_s \times P_s \times 100}{R_s \times C_u \times 1{,}000}$$

$$\text{L} = \text{Percent largest related compound} = \frac{L_u \times C_s \times P_s \times 100}{R_s \times C_u \times 1{,}000}$$

where:

A_u=Area of the tetrazole sample peak;

A_s=Area of the tetrazole working standard peak;

C_s=Concentration of the working standard in milligrams per milliliter;

P_s=Potency of the working standard in micrograms per milligram;

C_u=Concentration of the sample solutions in milligrams per milliliter;

R_u=Sum of peak areas of other compounds, excepting MMT and cefpiramide, detected in the sample chromatogram.

R_s=Area of the cefpiramide working standard peak; and

L_u=Area of the largest related peak, except MMT.

T=Percent total related compounds=$T_1 + T_2$.

(5) *Specific rotation.* Dilute an accurately weighed sample with sufficient dimethylformamide to obtain a concentration of approximately 10 milligrams of cefpiramide per milliliter. Proceed as directed in §436.210 of this chapter, using a 1-decimeter polarimeter tube. Calculate the specific rotation on the anhydrous basis.

(6) *Identify.* Proceed as directed in §436.211 of this chapter using a 1-percent potassium bromide disc prepared as directed in §436.211(b)(1).

(7) *Chrystallinity.* Proceed as directed in §436.203(a) of this chapter.

[55 FR 14240, Apr. 17, 1990]

§442.69 Cefmetazole.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefmetazole is (6*R*,7*S*)-7-[2-[(cyanomethyl)thio]acetamido]-7-methoxy-3-[[(1-methyl-1*H*-tetrazol-5-yl)thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid. It is so purified and dried that:

(i) Its potency is not less than 970 micrograms of cefmetazole activity per milligram.

(ii) Its moisture content is not more than 0.5 percent.

(iii) It gives a positive identity test for cefmetazole.

(2) *Labeling.* It shall be labeled in accordance with the requirements of §432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, moisture, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research: 10 packages each containing approximately 500 milligrams.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in §442.70a(b)(1).

(2) *Moisture.* Proceed as directed in §436.201 of this chapter.

(3) *Identity.* Proceed as directed in §436.211 of this chapter using a mineral oil mull prepared as described in paragraph (b)(2) of that section.

[59 FR 12546, Mar. 17, 1994]

§442.70a Sterile cefmetazole sodium.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Sterile cefmetazole sodium is the sodium salt of (6*R*-cis)-7-[[[cyanomethyl)thio]acetyl]amino]-7-methoxy-3-[[(1-methyl-1*H*-tetrazol-5-yl)thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid. It is a lyophilized powder. It is so purified and dried that:

(i) If the cefmetazole sodium is not packaged for dispensing, its cefmetazole potency is not less than 860 micrograms and not more than 1,003 micrograms of cefmetazole activity per milligram on an anhydrous basis. If the cefmetazole sodium is packaged for dispensing, its cefmetazole potency is not less than 860 micrograms and not more than 1,003 micrograms of cefmetazole activity per milligram on an anhydrous basis and also, each container contains not less than 90 percent and not more than 120 percent of the number of milligrams of cefmetazole that it is represented to contain.

(ii) It is sterile.

(iii) It contains not more than 0.2 endotoxin units per milligram.

(iv) Its moisture content is not more than 0.5 percent.

(v) The pH of an aqueous solution containing 100 milligrams per milliliter is not less than 4.2 and not more than 6.2.

(vi) It gives a positive identity test.

(2) *Labeling.* It shall be labeled in accordance with the requirements of §432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for cefmetazole potenty and content (if packaged for dispensing), sterility, bacterial endotoxins, moisture, pH, and identity.

(ii) Samples, if required by the Center for Drug Evaluation and Research:

(A) If the batch is packaged for repacking or for use as an ingredient in the manufacture of another drug:

(*1*) For all tests except sterility: 10 packages, each containing approximately 500 milligrams.

(*2*) For sterility testing: 20 packages, each containing equal portions of approximately 300 milligrams.

(B) If the batch is packaged for dispensing:

(*1*) For all tests except sterility: A minimum of 10 immediate containers of the batch.

(*2*) For sterility testing: 20 immediate containers collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in §436.216 of this chapter, using ambient temperature, an ultraviolet detection system operating at a wavelength of 214 nanometers, a 25-centimeter X 4.0- or 4.6-millimeter (inside diameter) column packed with microparticulate (5 micrometers in diameter) reversed phase packing material such as octadecyl silane bonded to silicas, a flow rate of not more than 2.0 milliliters per minute, and a known injection volume of between 10 and 20 microliters. Mobile phase, working standard and sample solutions, resolution test solution, system suitability requirements, and calculations are as follows:

(i) *Mobile phase.* Transfer 5.75 grams of ammonium dihydrogen phosphate to a 1-liter container. Add 700 milliliters of deionized water and agitate to aid dissolution. Transfer 3.2 milliliters of 40 percent tetrabutylammonium hydroxide (TBAH) in distilled water to the solution and shake. Add 280 milliliters of methanol and a range 20 to 30 milliliters of tetrahydrofuran and mix well. Adjust the pH to 4.5±0.1 with phosphoric acid. The mobile phase is 0.05*M* ammonium dihydrogen phosphate: methanol: tetrahydrofuran (700:280:20–30). It is 0.005*M* with respect to TBAH. Filter the mobile phase through a suitable filter capable of removing particulate matter to 0.5 micron in diameter and degas it just prior to its introduction into the chromatograph.

(ii) *Preparation of working standard, sample, and resolution test solutions*—(A) *Working standard solution.* Dissolve and